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14. ABSTRACT

Interventions to maintain performance are necessary to meet demanding mission requirements during sustained and surge aviation operations. Tube foods are the only foods that can be consumed during a U-2 mission due to the confining and encapsulating nature of required support equipment. Caffeine is a safe and effective strategy to enhance cognitive performance and is an ingredient in some tube foods. The objective of this study was to determine whether moderate doses of caffeinated tube foods would enhance performance in a simulated U-2 mission. ***Methods:*** Volunteers were 12 healthy USAF male pilots. The study used a double blind, placebo-controlled, two-factor, repeated measures (five iterations per night) design. Caffeinated (200 mg each) or placebo tube food was consumed at 00:00 and 04:00. Dependent measures assessed included standardized tests of cognitive performance, vigilance, and mood designed to simulate the demands of a nighttime U-2 mission. ***Results:*** Statistically significant ($p < 0.05$) improvements in performance due to caffeine administration compared with placebo were present in all five cognitive tasks either as main effects, interactions, or absence of significant degradation in the caffeine treatment condition compared with the placebo condition. A majority of sleep deprivation-induced performance decrements were attenuated by 200 mg of caffeine in tube food consumed every 4 h, and in some cases, performance was improved beyond baseline levels. ***Conclusions:*** Caffeinated tube food maintained cognitive performance representative of U-2 long-duration mission tasks at or near baseline levels for a 9-h overnight period in qualified USAF pilots. Side effects were minor and did not differ between placebo and caffeine conditions.

15. SUBJECT TERMS
Caffeine, fatigue, U-2, sleep deprivation, cognitive performance, vigilance, encapsulation

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Caffeinated Tube Food Effect on Pilot Performance During a 9-Hour, Simulated Nighttime U-2 Mission

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Doan BK, Hickey PA, Lieberman HR, Fischer JR. ***Caffeinated tube food effect on pilot performance during a 9-hour, simulated nighttime U-2 mission.*** **Aviat Space Environ Med 2006; 77:1034–40.**

Introduction: Interventions to maintain performance are necessary to meet demanding mission requirements during sustained and surge aviation operations. Tube foods are the only foods that can be consumed during a U-2 mission due to the confining and encapsulating nature of required support equipment. Caffeine is a safe and effective strategy to enhance cognitive performance and is an ingredient in some tube foods. The objective of this study was to determine whether moderate doses of caffeinated tube foods would enhance performance in a simulated U-2 mission. ***Methods:*** Volunteers were 12 healthy USAF male pilots. The study used a double blind, placebo-controlled, two-factor, repeated-measures (five iterations per night) design. Caffeinated (200 mg each) or placebo tube food was consumed at 00:00 and 04:00. Dependent measures assessed included standardized tests of cognitive performance, vigilance, and mood designed to simulate the demands of a nighttime U-2 mission. ***Results:*** Statistically significant ($p < 0.05$) improvements in performance due to caffeine administration compared with placebo were present in all five cognitive tasks either as main effects, interactions, or absence of significant degradation in the caffeine treatment condition compared with the placebo condition. A majority of sleep deprivation-induced performance decrements were attenuated by 200 mg of caffeine in tube food consumed every 4 h, and in some cases, performance was improved beyond baseline levels. ***Conclusions:*** Caffeinated tube food maintained cognitive performance representative of U-2 long-duration mission tasks at or near baseline levels for a 9-h overnight period in qualified USAF pilots. Side effects were minor and did not differ between placebo and caffeine conditions.

Keywords: caffeine, fatigue, U-2, sleep deprivation, cognitive performance, vigilance, encapsulation.

SUBSTANTIAL DECREMENTS in cognitive function resulting from continuous, or sustained, operations have long been documented (12); however, non-sleep deprived warfighters who are required to maintain alertness for long periods of time are also susceptible to significant deterioration in key aspects of cognitive performance, particularly vigilance (9–11). As sleep deprivation is often one of the prime limiters of performance, use of alertness-enhancing fatigue countermeasures such as dextroamphetamine and modafinil have become common in military settings (4) beyond good sleep hygiene and optimal scheduling.

One countermeasure that could be employed in a commercial and military setting is caffeine. As one of the most widely consumed stimulants in the world, caffeine is generally viewed as safe. Readily available in foods, over-the-counter medications, gum, and candy, caffeine is a prime candidate for strategic use as a fatigue countermeasure. Beneficial effects of caffeine are present across a wide range of doses (32–600 mg) and appear to be independent of sensory modality, having been documented by both visual and auditory vigilance tasks (1,8–11). Also, caffeine has been demonstrated to be a safe and effective strategy to enhance cognitive performance (11,19,22).

In rested volunteers, the effects of caffeine are largely limited to cognitive tasks that require sustained attention, particularly vigilance (11,19); whereas, in sleep-deprived individuals, the beneficial effects of caffeine generalize to a wide variety of cognitive tasks in addition to enhancing vigilance. For example, in a study conducted with sleep-deprived volunteers at the Walter Reed Army Institute of Research, doses of 150, 300, and 600 mg of caffeine per 70 kg of bodyweight significantly improved several aspects of cognitive performance without producing any adverse effects (18). In addition, Johnson and colleagues (9,10) demonstrated (using a rifle marksmanship simulator and simulated sentry duty task lasting several hours) that 200 mg of caffeine enhanced performance in rested volunteers. In these studies, 200 mg of caffeine improved speed of target detection with no reduction in accuracy (9,10). Deslandes et al. (6) demonstrated that 400 mg of caffeine produced significant electrophysiological changes in rested individuals, while changes in standard cognitive measures showed no change.

In a study designed to assess caffeine in highly stressful, combat-like conditions, Lieberman et al. (15) studied sleep deprived and environmentally stressed volunteers (SEAL trainees during Hell Week) and demonstrated that caffeine enhanced vigilance and other aspects of cognitive performance. In that study,

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caffeine in doses of 100, 200, and 300 mg was tested and no adverse effects on a task requiring fine motor control (marksmanship), or on mood states such as anxiety, were observed (15). The optimal dose of caffeine in those circumstances was judged to be 200 mg. This is the same dose present in most over-the-counter alertness enhancing products.

Caffeine has been extensively studied in liquid, pill, and gum formulations. However, we could not find any published literature on the effects of caffeine in food form. The pharmacokinetics and effects of caffeine in food form will likely be different. Additionally, there has been no research evaluating the effects of caffeine on pilots and simulated piloting skills.

The objective of the present study was to determine whether moderate doses of caffeine contained in tube foods could enhance cognitive performance in a laboratory study designed to simulate the cognitive demands of a U-2 mission. Focus groups conducted with operational U-2 pilots suggest they have difficulties maintaining the required levels of alertness during many missions. Pilot sleep loss is often unavoidable in typical U-2 operations, as well as other military aviation missions. The USAF Safety Center has noted pilot sleep deprivation as a causal or contributory factor in 8% of Class A mishaps, costing the Air Force millions of dollars annually in personnel, weapon systems, and property losses (21).

Although this study focused on application of caffeinated tube food for long-duration U-2 night missions, caffeinated tube food has potential applications to other populations who wear complex protective clothing, such as chemical warfare protective or spacesuits, for extended work periods. The study hypothesis was vigilance, cognitive performance, and basic flight skills would be impacted adversely in untreated subjects (i.e., placebo condition) as the result of the interactive influences of fatigue due to sleep deprivation and the nighttime circadian nadir of cognitive performance. In addition, it was hypothesized that this negative impact on vigilance, cognitive performance, and basic flight skills would be attenuated in subjects ingesting caffeinated tube food.

METHODS

Participants

There were 12 male USAF pilots (11 T-38 pilots and 1 F-16 pilot) who were recruited from local Air Force installations (26–45 yr old). Volunteers who met study qualifications completed all data collection at the Fatigue Countermeasures Lab located on Brooks-City Base in San Antonio, TX. Any individual with known hypersensitivity to caffeine, other xanthines, or suffering from hypertension or cardiovascular disease was excluded from participation. All participants were briefed on the important elements of the protocol, read, and later signed the informed consent document approved by the Brooks City-Base and USAF Surgeon General's Human Use Committee (protocol no. FBR-2003–30H). Participants were on leave status during the study and were provided monetary compensation for their time.

Data Collection

The experiment used a double blind, repeated-measures design with two within-subject factors: drug condition (caffeine or placebo) and time (five 2-h test blocks). Each subject received both treatment conditions, spaced by at least 1 wk, with the order of presentation being randomized and counterbalanced. Each participant completed three 3-h training sessions prior to 2 nights of actual testing, which insured stable and consistent performance was achieved for each of the cognitive and physiological test measures. Participants were issued wrist activity monitors to measure patterns of activity and sleep 1 wk prior to each testing session. On the morning of each testing session, participants were instructed to awaken no later than 07:00, perform their normal daily activities, and refrain from napping, nicotine, or caffeine use. At 21:30 the participants reported to the laboratory.

Each night of testing, participants completed five testing blocks that occurred at 22:00 (baseline trial), 00:00 (first dose), 02:00, 04:00 (second dose), and 06:00. Each dose of tube food contained either caffeinated chocolate pudding (200 mg) or plain chocolate pudding. These doses were consumed 15 min prior to the second and fifth test blocks. During each test block, participants performed a desktop flight simulator task, mood survey, symptom questionnaire, and various cognitive tasks. Each test block took the participants an average of 106 min to complete, so there was a supervised 24-min break at the end of each test block. Participants were monitored at all times to prevent napping or caffeine intake during testing sessions.

Cognitive Tests

The cognitive test battery duration (not including the Scanning Visual Vigilance Test, which lasted 30 min) lasted 18–20 min for each administration and was based on a cognitive task analysis of a typical U-2 mission. See Doan et al. (7) for details of the cognitive task analysis. Each individual test lasted up to 3 min. The battery used tests similar to those used previously to monitor performance decrements due to sleep deprivation (20) and the effects of stimulants (3).

The Adaptive Tracking Task required participants to maintain a vertical line within a horizontal plane located in the center of the computer screen. The task became more difficult as time progressed. The principal outcome measure for this task was root mean square error.

The Code Substitution Task was used to assess short-term memory function. Participants were required to memorize a list of symbols and associated numbers. Subsequently a symbol/number pair was displayed and the participants were required to identify the probe as correct or incorrect. The principal outcome measure was throughput (number of correct responses per minute).

The Match-to-Sample Task displayed a sample 4 × 4 matrix containing a pattern of red and blue boxes for 3 s. Participants were then required to choose from two new matrices where one matched the original. The principal outcome measure for this task was throughput.

The Nova Scan™ is a complex task and requires participants to perform three distinct sub-tasks, two of which occurred simultaneously. A gauge-monitoring task was always present while the primary task randomly changed from a continuous memory task to a working memory and spatial visualization (manikin) task. The principal outcome measure for this task was the mean response time to the transition trials which alternated between the continuous memory and manikin tasks.

The Scanning Visual Vigilance Test has been used previously to detect effects of moderate doses of caffeine on vigilance (8,13–14). The task required the volunteer to detect a faint dot that randomly appeared in an arbitrary point on the screen for 2 s. Individual volunteers' visual thresholds were obtained prior to actual testing. Average presentation of the dot occurred once a minute. On detection of the stimulus, the volunteer pressed the space bar on the keyboard as quickly as possible. The computer recorded whether each stimulus was detected and response time for detections. Responses made before or after stimulus occurrence were recorded as false alarms. The number of hits (correct responses) was the primary outcome measure for this task.

Questionnaires

A background questionnaire was administered once during a practice session to obtain basic descriptive data such as age, height, weight, etc. Background questions regarding demographic information such as military rank, ethnic group, and time on active duty, etc. were also obtained. In addition, prior and current levels of caffeine consumption and tobacco use were obtained. To avoid tolerance and withdrawal effects, individuals with excessive caffeine and nicotine consumption habits were not allowed to volunteer for the study.

The Profile of Mood States (17) was administered once per test block. Participants rated a series of 65 mood-related adjectives on a 5-point scale. Scores for six mood factors (anger, confusion, depression, fatigue, tension, and vigor) were the primary outcome measures.

Participants documented their fatigue state every 2 h during the study, as well as their sleep history, on an activity log. The log was used for a week prior to the first test session to help assure that none of the volunteers had atypical sleep activity patterns. They also completed the log during the weeks between test sessions and for a week after the final test session.

A 73-item symptom questionnaire was administered during each test block. Participants were asked to circle the appropriate rating (none, slight, moderate, or severe) for each of the symptoms listed. In addition, participants were asked once at the end of each test session whether they thought they had received caffeine.

Actigraphy

Participants wore actigraphs (MiniMitter Actiwatch, Mini-Mitter Co., Inc., Bend, OR) for a week prior to the first test session, between test sessions, and for 3 d following the final session to assure that they did not have atypical sleep activity patterns, and to quantify recovery sleep. An accelerometer recorded the individual's movements over time while awake and during sleep (5). None of the participants slept for less than 6 h any night 1 wk prior to either experimental session, which agreed with the activity log data. Therefore, no participant was dropped from the study due to atypical sleep patterns.

Caffeinated Tube Food

Each individual dose of caffeine administered in this study (200 mg) was equivalent to approximately two cups of strong coffee (2). A recommended dose of caffeine given as an over-the-counter stimulant is 200 mg every 3–4 h. The total dose of 400 mg administered in this study (two 200-mg doses over 4 h) was, therefore, within normally accepted limits.

Data Analysis

Prior to statistical analysis, the data were baseline-adjusted to counter any potential change in a participant's performance from the first experimental session to the second. This was accomplished for each outcome measure by subtracting a participant's data at baseline (Day 1, 22:00) from the data at each of the five trials. For each outcome measure, a repeated-measures analysis of variance (ANOVA) was performed to test for significant drug main effects, time main effects, and drug-by-time interaction. A Huyhn-Feldt adjustment to degrees of freedom was made for variables that failed Mauchly's Test of Sphericity. When significant effects were detected in the ANOVAs, post hoc simple effects tests were used to compare change from baseline under caffeine with change from baseline under placebo, at each time point, separately. In addition, the mean at each time point was compared with the mean at baseline for the placebo and caffeine treatment conditions.

Power Analysis

All testing was performed at the 0.05 α level. The primary goal of the study was to determine whether there was a difference between placebo and caffeinated tube food conditions during 1 night of sleep loss. Consequently, the power analysis was based on the specific post hoc comparisons of the two drug conditions. The sample of 12 complete data sets provided a 90% chance (power) of detecting a difference that is about one SD of the difference in magnitude (i.e., effect size of 1.0).

RESULTS

All 12 participants completed the study. Due to occasional technical problems, a small amount of data was lost (less than 2%). Prior to analysis, we estimated each missing point based on the average percent change of

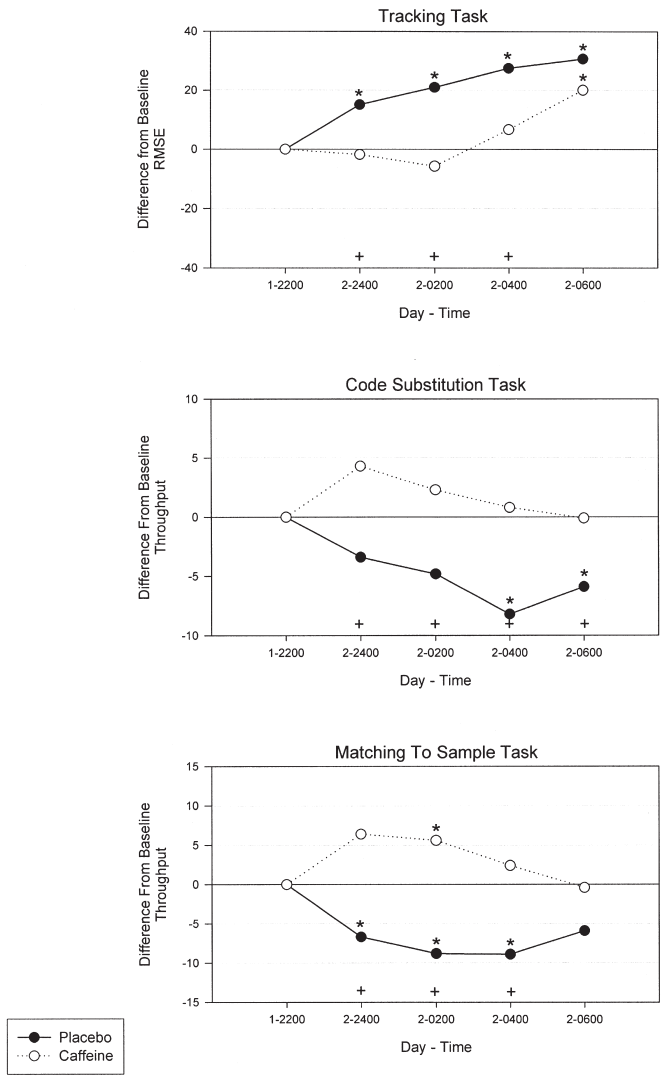

Fig. 1. All values are mean differences from baseline time off target in milliseconds. * Significant difference from baseline ($p \leq 0.05$); + significant drug difference ($p \leq 0.05$). Tracking baseline values: 54.48 rmse (placebo), 55.19 rmse (caffeine). Code Substitution baseline values: 55.4 (placebo), 54.6 (caffeine). Matching to Sample baseline values: 49.6 (placebo), 47.6 (caffeine).

the other data available for that same drug condition and time point (for the ANOVAs, degrees of freedom for drug by time error terms were reduced by the number of missing points estimated).

For the Adaptive Tracking Test, significant main effects for drug [MSE = 453.06, F (1,11) = 14.96, p = 0.003], time [MSE = 274.86, F (4,44) = 8.66, $p < 0.001$], and a drug-by-time interaction [MSE = 247.038, $F(3,29)_{HF\ adjusted} = 3.67$, p = 0.038] were detected for root mean square error. Performance in the placebo condition degraded from baseline over time, while performance in the caffeine condition remained near baseline levels until 06:00 (**Fig. 1**).

For the Code Substitution Test, significant main effects for drug [MSE = 68.65, F (1,11) = 15.25, p = 0.002], time [MSE = 23.73, F (4,44) = 3.36, p = 0.017], and a drug-by-time interaction [MSE = 23.75, F (4,42) = 3.03, p = 0.027] were detected for throughput (correct responses per minute of correct responding). Performance during placebo treatment degraded over time while performance in the caffeine condition was above or at baseline performance for the duration of the session (Fig. 1).

For the Match-to-Sample Test, a significant main effect for drug [MSE = 195.26, F (1,11) = 12.06, p = 0.005] and a significant drug-by-time interaction [MSE = 23.75, F (4,42) = 5.47, p = 0.002] were observed for throughput. Performance in the placebo condition degraded while performance in the caffeine condition improved, or remained near baseline for all trials (Fig. 1).

For the Nova Scan Test, significant main effects for drug [MSE = 41065, F (1,11) = 12.94, p = 0.004] were detected for mean response time to the transition trials. Performance in the placebo condition generally degraded while performance in the caffeine condition improved, or remained near baseline for all trials (**Fig. 2**).

For the Scanning Visual Vigilance Test, three subjects had to be dropped due to failure to complete at least one of the trials. Analyses were performed on the remaining nine subjects. Significant main effects for time

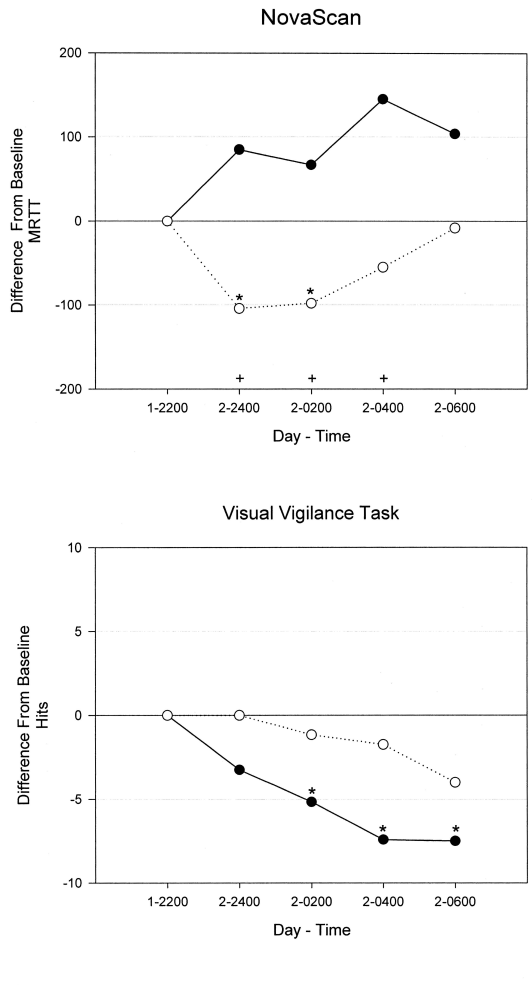

Fig. 2. All values are mean differences from baseline. * Significant difference from baseline ($p \leq 0.05$); + significant drug difference ($p \leq 0.05$). NovaScan baseline values: 1897 ms (placebo), 1908 ms (caffeine). Visual Vigilance baseline values: 18.00 (placebo), 14.25 (caffeine).

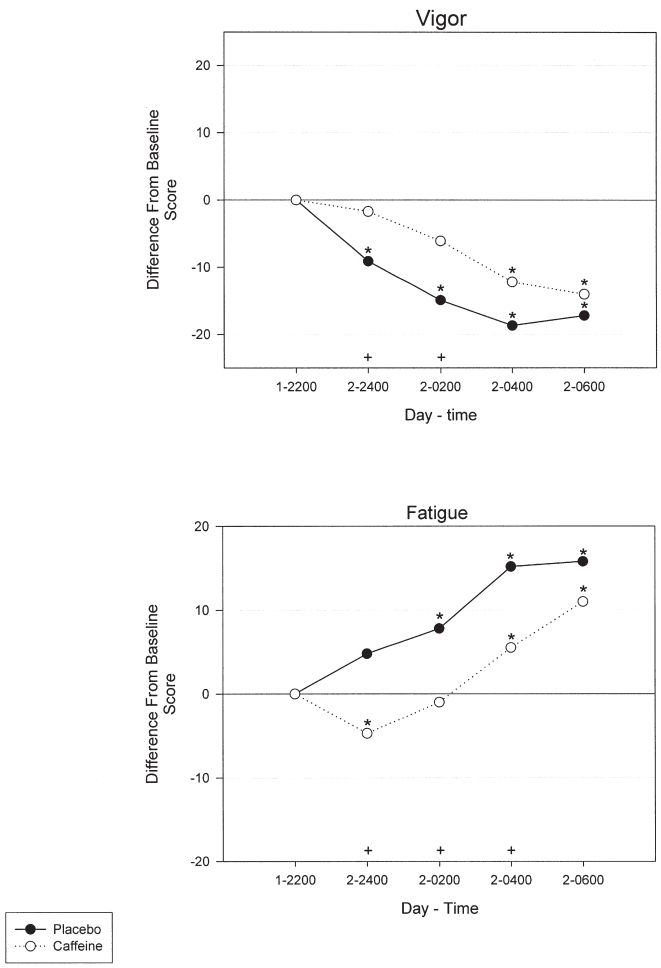

Fig. 3. All values are mean differences from baseline. * Significant difference from baseline ($p \leq 0.05$); + significant drug difference ($p \leq 0.05$). Vigor baseline values: 51.6 (placebo), 51.8 (caffeine). Fatigue baseline values: 45.8 (placebo), 44.1 (caffeine).

[MSE = 23.97, F (4,32) = 6.60, p = 0.001] were detected for the number of hits (correct responses). The number of hits decreased over time for both conditions, but significant decreases were seen only for the placebo condition (Fig. 2).

For the Profile of Mood States, significant drug-by-time interactions were detected for the fatigue [MSE = 16.89, F (4,44) = 6.18, $p < 0.001$] and vigor [MSE = 27.27, F (4,44) = 2.77, p = 0.039] scales. There was also a drug main effect for fatigue [MSE = 60.58, F (1,11) = 21.35, p = 0.001], and time main effects for both fatigue [MSE = 51.39, F $(3,28)_{HF\ adjusted}$ = 27.66, $p < 0.001$] and vigor [MSE = 30.85, F (4,44) = 35.25, $p < 0.001$]. Mood in the placebo condition generally degraded while mood in the caffeine condition remained near baseline through the first two trials following baseline testing (**Fig. 3**).

None of the participants reported moderate or severe symptoms in the caffeine or placebo condition, but a modest increase in some symptoms in both conditions was present. **Table I** shows, for each symptom, the number of participants for whom the symptom was worse (though still slight) during the night than it was at baseline. Symptoms never reported in either condition were omitted from Table I.

DISCUSSION

Caffeine has been studied extensively (11,18), but to the best of our knowledge, this is the first investigation of the effects of a caffeinated food, as opposed to a beverage, on performance. Additionally, caffeine has not been studied in a simulated aviation environment. The duration of testing and the specific cognitive tests used in this investigation were specifically designed to replicate the cognitive demands of the U-2 environment. Additionally, this is the first investigation to assess the effects of caffeine in actual USAF pilots in a mission-relevant environment.

TABLE I. NUMBER OF PARTICIPANTS FOR WHOM THE SYMPTOM WAS WORSE THAN AT BASELINE.

Symptom	Caffeine	Placebo	Symptom	Caffeine	Placebo
Abdominal Pain	3	0	Irritable	3	1
Awareness of Breathing	2	0	Itching	2	1
Chest Pain	1	0	Loss of Balance	1	2
Confusion	0	1	Loss of Coordination	2	6
Difficulty Focusing	4	8	Memory Loss	0	1
Diarrhea	1	0	Mentally Depressed	0	1
Difficulty Staying Awake	10	9	Muscle Cramp	1	0
Difficulty Concentrating	7	11	Nasal Congestion	0	1
Dizzy with Eyes Closed	1	2	Nausea	2	1
Dizzy with Eyes Open	2	3	Nervous	1	0
Drowsiness	8	10	Numbness	1	0
Drugged Feeling	2	2	Rash	1	0
Eye Strain	2	4	Shortness of Breath	0	1
Fatigued	9	11	Sore Throat	1	0
Frequent Urination	3	3	Stomach Awareness	3	1
Full-Headed Feeling	0	1	Stomach Cramp	4	1
General Discomfort	3	2	Swelling	1	0
Headache	1	0	Thirst	0	1
Increased Appetite	0	1	Tingling	1	0
Increased Saliva	0	1	Vertigo	0	1
Irregular Heart Rate	1	0	Visual Illusions	1	1

The objective of this study was to determine whether moderate doses of caffeine formulated in tube foods could enhance cognitive performance in a laboratory study designed to simulate the cognitive demands of a U-2 mission. Due to the pressure suit required for high-altitude operations, tube foods are the only foods that can be consumed during a U-2 mission. These foods are prepared by the Department of Defense combat feeding program at the Natick Soldier Systems Center. The Natick Combat feeding program was tasked to provide the U-2 program with tube foods that enhance performance. The AF Food Service Directorate of Operations requested a study to determine whether the caffeine-containing tube foods produced by Natick Soldier Systems Center enhance vigilance and cognitive performance.

The cognitive performance and mood data from this investigation support the hypothesis that caffeinated tube food attenuates some performance decrements associated with sleep loss. Statistically significant improvements in performance due to caffeine administration compared with placebo were present in all five cognitive tasks either as main effects, interactions, or absence of significant degradation in the caffeine treatment condition compared with the placebo condition. The two doses of 200 mg of caffeine in the tube food were sufficient to attenuate a majority of the sleep deprivation-induced performance decrements and, in some cases, even improve performance beyond baseline levels, particularly at the 00:00 and 02:00 time points.

The Scanning Visual Vigilance Test previously has been shown to be sensitive to effects of moderate doses of caffeine on vigilance (16). Although there was an absence of significant degradation in the caffeine treatment condition compared with the placebo condition in the present study, there was not a drug main effect. One possible explanation for this disparity in results is increased variation in the present study due to lack of volunteer motivation. Participants repeatedly complained about the long, boring nature of the Scanning Visual Vigilance Test relative to the other tasks in this present study and, therefore, may not have exerted maximal effort.

Because of the small sample size, conducting nonparametric statistical testing would not produce meaningful results for the symptom questionnaire data. However, an increase in the number of reports of abdominal pain and cramping under the caffeine condition was observed. It is important to note that only the lowest level of intensity (slight) was indicated by the participants under either condition. In fact, not one of the 73 symptoms was ever reported as greater than 'slight.'

Further research should be conducted to compare the pharmacokinetics of caffeinated food to liquids, pills, and gum. When caffeine is administered in food, this may slow its absorption and delay and sustain its effects. This pharmacokinetic profile may be preferable for certain applications. Additionally, further study of caffeinated tube food should be conducted in more real world like settings, such as aircraft simulators, aircraft in flight, and in other military situations that require complex protective clothing such as chemical defense suits.

Conclusions

In tasks representative of those used during a U-2 long-duration mission, two doses of 200 mg caffeinated tube food maintained cognitive performance above or near baseline levels for a 9-h overnight period in a group of 12 qualified USAF pilots. In many cases, performance was improved beyond baseline levels, particularly at the 00:00 and 02:00 time points. Side effects were rarely reported and were only 'slight' in severity under both the placebo and drug conditions. Based on the results from this investigation, caffeinated tube food is an effective tool for sustaining cognitive performance and vigilance during extended and nighttime U-2 operations. Results may also be generalized to other populations who wear complex protective clothing, such as chemical warfare protective or spacesuits, for extended work periods.

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